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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/470,944	12/22/99	GUNDLING	G 6653.US.01

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EXAMINER	
SPIEGLER, A	
ART UNIT	**PAPER NUMBER**
1656	15

DATE MAILED: 09/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/470,944	GUNDLING, GERARD	
	Examiner	Art Unit	
	Alexander H. Spiegler	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *07 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. The request filed on August 7th, 2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/470,944 is acceptable and a CPA has been established. An action on the CPA follows.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1 and 5-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uematsu et al. (EP 0757106 A2, 1997), and further in view of Kim et al. (WO 92/18514).

Uematsu et al. disclose a method for isolating a nucleic acid by mixing a metal oxide support, a material containing a nucleic acid, and a solution for extracting the nucleic acid forming a sample solution, separating the metal oxide support to which the nucleic acid has been bonded from the sample solution, and eluting the nucleic acid from the magnetic carrier to which the nucleic acid has been bonded (pg. 3, ln. 42-45). Uematsu et al. further teach that the solution used in the extraction of the nucleic acid contains a buffer containing a chaotropic material, such as guanidine salts, potassium iodide, sodium thiocyanate, sodium isothiocyanate, and urea (pg. 5, ln. 54-56). Furthermore, the reference teaches that the buffer can be used in combination with Triton X-100, a known detergent, and Tris HCl buffer (pg. 5, ln.56 - pg.6 ln. 1). With respect to claim 5, the reference further teaches a wash step of an aqueous solution of about 70% ethanol, following the separation of the metal oxide support/nucleic acid complex from the sample

solution (pg.5, 43-44). With respect to claim 6, Uematsu et al. teach that following the wash step the nucleic acid is then eluted form the metal oxide support, with a Tris-EDTA bufer (TE buffer), or sterilized water (pg. 5, ln. 45). With respect to claim 7, the reference further teaches the detection of the nucleic acid after eluting the nucleic acid from the metal oxide support (pg. 3, ln. 57 - pg. 4, ln. 6). With respect to claim 8, the reference further teaches the step of amplifying the eluted nucleic acid (pg. 4, ln. 8-9). With respect to claim 9 and 10, the reference teaches that the nucleic acid used is RNA or DNA, and is taken from a biological source (i.e. whole blood, urine) (pg. 2-3). Uematsu et al. teach a kit for isolating nucleic acid comprising a metal oxide support and a solution for extracting the nucleic acid, which is composed of a chaotropic agent, a detergent, and an elution buffer comprising water (pg. 4, ln. 10-12). With respect to claim 12, the reference teaches (pg. 14, ln. 34-35) teaches the amplification of the nucleic acid without the removal of the elution buffer. With respect to claims 13-14, Uematsu teaches the elution of the nucleic acid can be conducted in a solution having a low ionic strength (for example, sterilized water, which has a pH of 7.0) (pg. 6, ln. 8-9). Uematsu does not teach that the nucleic acid bonds with the metal oxide support material.

Kim teaches the purification of nucleic acids using metal oxide supports. Specifically, the reference teaches the bonding of nucleic acid directly to a metal oxide support material (pg. 7, ln. 11-25), which provides the advantage in that the bonded nucleic acids can be readily isolated (pg. 3, ln. 14-21), and provides the benefits of an optimal combination of such properties as recovery, relative purity, and biological activity of the recovered nucleic acid, as well as, versatility, cost, speed, simplicity, and ease of use (pg. 3, ln. 31-35). The reference also teaches that any biological sample containing the desired nucleic acids (pg. 3, ln. 22-30). With respect to

claims 15-16, Kim teaches the elution of a bound nucleic acid from a metal oxide support material using potassium phosphate (Example 5, pgs. 17-18). In particular, Kim teaches that 30mM potassium phosphate is effective to recover 86% of bound DNA (pg. 17).

In view of the teachings of Kim, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Uematsu so as to have performed the method of separating nucleic acids from a test sample through the bonding of the nucleic acid to a metal oxide support material, in order to have achieved the benefit of providing a more versatile, cost-effective, and more efficient means of separation. With respect to claim 11, the references do not teach a kit comprising, a metal oxide particle (which bonds with a nucleic acid), a binding buffer (comprising a chaotropic agent and detergent), and an elution buffer). However, reagent kits for performing DNA isolation assays were conventional in the field of molecular biology at the time the invention was made. In particular, kits provide the advantage of pre-assembling the specific reagents required to perform an assay and ensure the quality and compatability of the reagents to be used in the assay. Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged a metal oxide particle (which bonds with a nucleic acid), a binding buffer (comprising a chaotropic agent and detergent), and an elution buffer), in a kit for the expected benefits of convenience and cost-effectiveness for practioners of the art. With respect to claims 15-16, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods of Uematsu et al. so as to have used an elution buffer which comprises potassium phosphate in place of TE buffer in order to have provided an equally

effective means for eluting the nucleic acids and providing a suitable medium for storing the eluted nucleic acid.

4. Claims 2-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uematsu et al. (EP 0757106 A2, 1997), in view of Kim et al. (WO 92/18514), as applied to claims 1 and 5-16 above, and further in view of Chomczynski (US 5945515).

The teachings of Uematsu and Kim are presented above. In particular, the references teach the isolation of nucleic acids by mixing a metal oxide support, a material containing a nucleic acid (i.e. bonding the nucleic acid to the metal oxide support material), and a solution for extracting the nucleic acid consisting of a buffer containing a chaotropic agent and a detergent, separating the metal oxide support to which the nucleic acid has been bonded from the sample solution, and eluting the nucleic acid from the magnetic carrier to which the nucleic acid has been bonded. The references do not teach a binding buffer further comprising an organic solvent and the flashpoint of the binding buffer is greater than 130 degrees Fahrenheit or the use of a reducing agent.

Chomczynski teaches a solution for isolation of RNA, DNA, and proteins from biological material, where the solution comprises a chaotropic agent, detergent, and organic solvent (col. 10, ln. 22-34). With respect to claim 3, Chomczynski teaches that the addition of substantially lower amounts of organic solvents are required to effect the precipitation of cellular components (col. 3, ln.65-68). With respect to claims 2 and 4, Chomczynski further teaches that the solution for the isolation of RNA, DNA, and proteins, also comprises a reducing agent (see abstract, and col. 4 ln. 4). Chomczynski teaches that the reducing agent facilitates denaturation of RNase by the chaotropes and aids in the isolation of undegraded RNA.

In view of the teachings of Chomczynski, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Uematsu and Kim so as to have added an organic solvent to a binding buffer comprising a chaotropic agent and a detergent, or a chaotropic agent, detergent, and reducing agent, in order to have achieved the benefit of effecting the precipitation of cellular components. With respect to claims 3 and 4, the resulting binding buffer containing low concentrations of organic solvent effective to precipitate the cellular components would be expected to have a flashpoint of greater than 130^0 F. With respect to claims 2 and 4, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Uematsu and Kim by adding a reducing agent to the binding buffer in order to have achieved the advantage stated by Chomczynski of enhancing the denaturation of RNase present in the sample thereby improving the isolation of RNA from the sample.

Conclusion

5. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Alexander H. Spiegler
September 4, 2001

CARLA J. MYERS
PRIMARY EXAMINER